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Massachusetts Department of Public Health
Minutes of the Drug Formulary Commission
Meeting of Thursday, May 5, 2016

Henry I. Bowditch Public Health Council Room, 2nd Floor
250 Washington Street, Boston, MA

Date of Meeting: Thursday, May 5, 2016
Beginning Time: 2:01 PM
Ending Time: 4:21 PM

Advisory Council Members Present: The following thirteen (13) appointed members of the Drug Formulary Commission attended on May 5, 2016, establishing the required simple majority quorum (9) pursuant to Massachusetts Open Meeting Law (OML): DPH Interim Director Bureau Health Care Safety and Quality Eric Sheehan (Chair); Dr. Douglas Brandoff; Ray Campbell; Dr. Daniel Carr; Dr. Joanne Doyle-Petrongolo; Dr. Ken Freedman; Dr. Paul Jeffrey; Dr. Virginia Lemay; Cindy Steinberg; Dr. Jeffrey Supko; Dr. Theoharis Theoharides; Ms. Tammy Thomas and Dr. Alexander Walker.

1. Welcome and Introductions

Department of Public Health (DPH) Bureau of Health Care Safety and Quality Interim Director Chair Eric Sheehan called the meeting to order at 2:01PM and provided brief introductory remarks.

Mr. Sheehan reminded the attendees that this is a recorded, public hearing, and confirmed that no one in audience was recording.

Mr. Sheehan summarized the April 7, 2016 meeting. He noted that the Commission at its last meeting began crosswalking the Abuse Deterrent Property (ADP) drug products it approved as potential substitutes with the drug products it determined have a Heightened Public Health Risk.

Data was presented on Embeda and several drug products for which it may be substituted, based on statutory criteria, and the definition approved for Chemically Equivalent Substitution and the form approved to determine the strength of evidence showing ADP Efficacy.

However, the Commission found that more data was needed to determine if the pairings fit the approved definition. In particular, the Commission determined that more data was needed to determine if the potential substitute produces a comparable biologic effect as the drug for which it was being considered as a substitute. This data will be presented today.

Mr. Sheehan called for approval of the minutes from the April 7, 2016 meeting.

- One typo was corrected by Dr. Carr. Dr. Carr also suggested edits to a statement by Dr. Jeffrey on page 5.
- Motion to approve: Ms. Steinberg
- Second: Dr. Carr
- All in favor: 8 in favor; 0 opposed; 3 abstention.
  Dr. Freedman, Dr. Lemay and Ms. Thomas abstained as they were not present at the April 7th meeting.

2. Crosswalk

Next, Mr. Sheehan reviewed the drugs on the 28 Heightened Public Health Risk drugs on List A and the five potential formulary substitutes on List B. Mr. Sheehan explained that the goal of the Crosswalk in Component 3 is to determine whether a drug product on List B should be a substitute for one or more drug products on List A. The Commission members were provided with complete lists, with accompanying cost and utilization data.

Mr. Sheehan stated that Section 13 of Chapter 17 of the General Laws guides the Commission's work in Component 3 by offering four criteria by which we determine that a drug is a chemically equivalent substitution. In addition to the definition of the term "chemically equivalent substitution" itself, the Commission must consider accessibility, cost, drug effectiveness, and ADP efficacy.

As the Commission evaluates each pairing based on these criteria, it is important to note that the totality of the factors should determine whether a List B drug product should substitute for a List A products. Factors should be considered in order for the Commission to meet its goal of finding safer alternatives for Heightened Public Health Risk Drugs. This is especially true of cost.

At the April 7th meeting, the members had several questions about the methodology and the completeness and relevance of the cost impact data. Karen Stevens, who attended the meeting on behalf of Tyson Thompson from UMass, provided an overview of the cost impact data.

Dr. Carr remarked on the cost methodology and noted that just because a drug is less expensive does not mean it should be prescribed over a more expensive drug.

Next, Jonathan Mundy introduced four pieces of pharmacokinetic data as requested by the members: Peak Concentration; Time to Peak Concentration; Elimination Half-Life; and Area Under the Curve (AUC). There was discussion on this data.

- Dr. Supko noted that AUC is a measure of absorption – comparable effect.
- Dr. Carr clarified that each drug was studied individually, and that no data from one informed the other. He noted, however, that this data gives a good ball park comparison.
- Dr. Steinberg asked about the perceived variation in the Embeda and Avinza data.

- Dr. Supko explained that different doses of the two drugs were studied.
- Ms. Steinberg asked for clarification on peak concentration and how quickly an individual may reach the amount of available drug.
- Dr. Theoharides advised members to keep in mind that the AUC similar for all but Avinza®.

Mr. Mundy introduced the potential pairing of Embeda, one of the List B drug products, and Morphine extended-release 24 hour capsule, a List A drug product. Mr. Mundy described the following information for each drug product: active ingredient; strength; dosage form; route of administration; dosing schedule; cost per unit; units dispensed in 2015; the approximate cost paid for these units; and the ADP efficacy category.

Following this review, the floor was opened for discussion. Commission members offered the following observations, comments, suggestions and recommendations:

- Dr. Carr noted that there may be drugs that aren't considered chemically equivalent under the Commission's purview or definition that could be flagged. There are factors that should be considered when looking at each drug. Mr. Sheehan stated that DPH could provide guidance once the Formulary is in place.
- Ms. Steinberg asked if the 178 patients noted on Slide 12 represent 100% conversion. Ms. Stevens replied that it does.
- Dr. Jeffrey asked about the difference in the drugs listed on slide 11 and those on the following slides. Ms. Stevens responded by explaining that each slide is comparing Embeda® to:
    - Slide 12 is generic Avinza®.
    - Slide 13 is Kadian®.
    - Slide 14 is generic Kadian®.
    - Slide 15 is MS Contin®.
    - Slide 16 is generic MS Contin®.
- Dr. Brandoff stated that he appreciated the additional data but emphasized that the ultimate caveat in working with individual patients is that you have to monitor the patient. The data shows that some patients will have different experiences which need to be monitored and adjusted, which is independent of whether or not the drug has ADPs. The data shows that the ultimate destination for patients is reasonably similar.
- Dr. Freedman asked for clarification on the cost of substitution on slide 12. Ms. Stevens explained that it included converting patients that were receiving generic Avinza®, or the morphine extended-release 24 hour capsule, to Embeda®.

Next, Mr. Mundy introduced the potential pairing of Embeda® and Kadian®. Mr. Mundy described the following information for each drug product: active ingredient; strength; dosage form; route of administration; dosing schedule; cost per unit; units dispensed in 2015; the approximate cost paid for these units; and the ADP efficacy category.

Following this review, the floor was opened for discussion. Ms. Steinberg asked why this substitution may result in cost avoidance. Ms. Stevens responded by explaining that this is one scenario where Kadian® is more expensive than Embeda®.

Mr. Mundy went through the information on the potential pairing of Embeda® and generic Kadian®, or the morphine extended-release 12 or 24 hour capsule. Mr. Mundy described the following information for each drug product: active ingredient; strength; dosage form; route of administration; dosing schedule; cost per unit; units dispensed in 2015; the approximate cost paid for these units; and the ADP efficacy category. There were no questions or discussion on this potential pairing.

Next, Mr. Mundy introduced the potential pairing of Embeda® and MS Contin®. Mr. Mundy described the following information for each drug product: active ingredient; strength; dosage form; route of administration; dosing schedule; cost per unit; units dispensed in 2015; the approximate cost paid for these units; and the ADP efficacy category.

Following this review, the floor was opened for discussion. Commission members offered the following observations, comments, suggestions and recommendations:

- Dr. Supko stated that he believes these are two different products with different properties. MS Contin® is faster acting.
- Dr. Walker asked if there will be another opportunity to compare or substitute a drug with ADPs for MS Contin®. Mr. Sheehan responded saying that it would not happen at this time. Ms. Steinberg stated that there are drugs in the FDA pipeline and we shouldn't substitute unless we are sure.
- Dr. Carr asked if we would be able to provide guidance to show that the Commission is aware of certain factors that should be taken into consideration when prescribing one of the drugs that is recommended for substitution. Mr. Sheehan stated that this was possible.

Mr. Mundy introduced the final potential pairing of Embeda® and generic MS Contin®, or the morphine extended-release tablet. Mr. Mundy described the following information for each drug product: active ingredient; strength; dosage form; route of administration; dosing schedule; cost per unit; units dispensed in 2015; the approximate cost paid for these units; and the ADP efficacy category.

Following this review, the floor was opened for discussion. Commission members offered the following observations, comments, suggestions and recommendations:

- Mr. Campbell asked what the 27,109 patients that were prescribed the generic MS Contin®, or the morphine extended-release tablet, in 2015 represented in terms of the percentage of total Prescription Monitoring Program (PMP) patients. Mr. Mundy stated that we do not have that information but this is a popular drug. It has been around for a long time and is easy to manipulate and abuse. It has a high-abuse potential.
- Dr. Walker stated that, in total, over 28,000 were prescribed the five drugs that are considered to be substituted by Embeda®. We are trying to save lives through the development of the Formulary. Dr. Walker expressed that expense of the substitution as equivalent to $2 million per life potentially saved by the substitution. If you look at the cost, we need to consider if each life is worth the cost of the substitution. If we

don't include this substitution but include the others, we still have a big problem because this is the number 1 abused drug. However, there needs to be a balance because they are not comparable.

- Dr. Brandoff stated that they may not be comparable but asked if they were inferior. For the cost of substitution, we need to look at who is paying for it. If we don't do the substitution, what other costs are being created? Dr. Brandoff urged the members not to look at the cost of the substitution in a vacuum, but to consider the cost of overdoses and substance use disorder treatment.
- Dr. Doyle-Petrongolo noted that the Formulary is supposed to be a guideline. It is not written in stone but provides an option. This doesn't have to be applicable to every person. The Commission was developed to look at these hard issues.
- Mr. Sheehan stated that prescribers know their patients. We are not telling them to change prescriptions but giving them a tool for them to use to address patients that are at risk of potential abuse.
- Dr. Freedman indicated that we need to consider that some of the patients that are currently prescribed the morphine extended-release tablet may switch to heroin. We need to make Formulary decisions that are in the best interest of the entire population and Commonwealth.
- Dr. Carr stated that this is not as simple as looking at the four pharmacokinetic data. There is room to recommend a switch in prescribing if a drug doesn't work for a patient, He noted the fact that this drug accumulates in the system, creating a "steady state".
- Dr. Jeffrey reminded the members that some people will also become addicted to Embeda, but if the Commission does not approve MS Contin and the generic, they will have done nothing.
- Dr. Theoharides asked about the source for the data for the morphine extended-release tablet. Ms. Stevens indicated that all data is from the FDA's website.

At this time, Mr. Sheehan asked the members if there were any more comments on each potential pairing before considering moving toward a vote on each.

- Dr. Jeffrey indicated that we do not have data on cost effectiveness of ADP drugs because they are too new. This is an area of emerging public policy about the way we value lives. We are reflecting on a greater charge.
- Dr. Walker asked if the Commission has the opportunity to impact the roll-out of the Formulary. Can we create categories or a tiering system of recommended substitutions? Mr. Sheehan responded by asking if tiered recommendations impact the prescriber/patient relationship.
    - Dr. Walker stated that this would help prescribing practices.
    - Dr. Brandoff noted that we need to provide guidance with instructions so prescribers are aware of the variables.
    - Dr. Doyle-Petrongolo described the "Beers Criteria" that is used for prescribing for the elderly. It has a tiered system.

Mr. Sheehan called for a break until 3:45 PM.

The meeting was called back to order at 3:50 PM.

Mr. Sheehan stated that the voting would begin with the possible substitution of Embeda® for the morphine extended-release 24 hour capsule. Dr. Carr asked what factors should be considered when voting. Mr. Sheehan responded that the totality of all the information presented should be considered.

Mr. Sheehan asked if there was a motion to approve Embeda® as a substitute for morphine extended-release 24 hour capsule.

- Motion to approve: Dr. Freedman
- Second: Dr. Jeffrey
- All in favor: 11 in favor; 1 abstention.
    - Ms. Thomas abstained.
- Dr. Carr stated that he wants to make sure the Formulary states that the substitutions are voluntary.

Mr. Sheehan stated that the next vote would be the possible substitution of Embeda® for Kadian®. Mr. Sheehan asked if there was a motion to approve Embeda® as a substitute for Kadian®.

- Motion to approve: Dr. Jeffrey
- Second: Dr. Theoharides
- All in favor: 11 in favor; 1 abstention.
    - Ms. Thomas abstained.

Mr. Sheehan stated that the next vote would be the possible substitution of Embeda® for the morphine extended-release 12 or 24 hour capsule. Mr. Sheehan asked if there was a motion to approve Embeda® as a substitute for the morphine extended-release 12 or 24 hour capsule.

- Motion to approve: Dr. Theoharides
- Second: Dr. Jeffrey
- All in favor: 11 in favor; 1 abstention.
    - Ms. Thomas abstained.

Mr. Sheehan stated that the next vote would be the possible substitution of Embeda® for MS Contin®.

- Dr. Supko stated that we know this substitution doesn't fit the definition. A 1:1 substitution doesn't match. It may be appropriate under a different definition but it doesn't fit this one.
- Dr. Theoharides asked if there could be consideration of approving the substitution with guidance. Mr. Sheehan noted that the motion could include the addition of guidance or advisory to be included. It could be the Commission's way to make sure guidance would be included.

- Dr. Supko indicated that we need to consider if other products come along through the FDA process. Mr. Sheehan stated that we could regularly update the guidance if something in the market changes. That's why the Commission will continue to meet.
- Dr. Theoharides noted that some members may feel more comfortable if we determined the language for the guidance now. Mr. Sheehan stated that it wasn't on the public agenda but we can do this at a future meeting.
- Dr. Supko stated that it is wrong to substitute products that are not bioequivalent. Physicians may think that they are comparable but it is misleading. This substitution would not get through the FDA.

Mr. Sheehan asked if there was a motion to approve Embeda® as a substitute for MS Contin® with additional guidance.

- Motion to approve: Dr. Walker
- Second: Dr. Freedman
- All in favor: 8 in favor; 3 in opposition; 1 abstention.
    - Dr. Jeffrey, Dr. Lemay and Dr. Supko voted in opposition.
    - Ms. Thomas abstained.

Mr. Sheehan stated that the next vote would be the possible substitution of Embeda® for the morphine extended-release tablet. Mr. Sheehan asked if there was a motion to approve Embeda® as a substitute for the morphine extended-release tablet with additional guidance.

- Motion to approve: Dr. Walker
- Second: Dr. Theoharides
- All in favor: 8 in favor; 3 in opposition; 1 abstention.
    - Dr. Jeffrey, Dr. Lemay and Dr. Supko voted in opposition.
    - Ms. Thomas abstained.

Dr. Walker asked if those that are in opposition to this pairing wanted to voice the reasons why they are opposed. Dr. Supko noted that he already stated his position.

Mr. Sheehan noted that for the next meeting, the Commission will go through a similar process for Oxaydo. We will review several potential pairings and discuss and vote on each option. We will also reconsider the monograph and other data relevant to your previous discussion on approval or rejection of Zohydro as a potential Component 3 substitute; and may proceed with the crosswalking of Hysingla.

Additionally, Mr. Sheehan indicated that the Commission will address its responsibilities under the Opioid Bill that was signed by the Governor in March. In upcoming meetings, the Commission will be presented with a potential list of FDA-approved non-opioid pain management alternatives with a lesser potential for abuse than Schedule II or III opioids, for your approval and publication.

DPH is working to identify additional meeting times in May, June and July. From the information that has been received, it is apparent that we will not have quorum for our next

scheduled meeting on May 19. The Commission is very close to finishing the draft Formulary and hope that everyone understands the sense of urgency to getting it done as soon as possible.

As part of closing remarks, Mr. Sheehan summarized the votes taken. The Commission voted to:

- Approve Embeda® as a chemically equivalent substitute for Morphine Extended-Release, 24-hour capsule.
- Approve Embeda® as a chemically equivalent substitute for Kadian®.
- Approve Embeda® as a chemically equivalent substitute for Morphine Extended-Release, 12 or 24-hour capsule, which is the generic for Kadian.
- Approve, with additional guidance, Embeda® as a chemically equivalent substitute for MS Contin®.
- Approve, with additional guidance, Embeda® as a chemically equivalent substitute for Morphine Extended-Release tablet, which is the generic for MS Contin®.

Having no further business before the Commission, Mr. Sheehan asked for a motion to adjourn.

- Motion: Dr. Jeffrey
- Second: Dr. Brandoff
- All in favor: unanimous

The Drug Formulary Commission meeting concluded at 4:21 PM.

Documents Presented to DFC at the *May 5, 2016* Meeting

- DFC Minutes from April 7, 2016
- DFC PowerPoint presentation
- Cost Information on Short-Acting and Long-Acting Opioids
- Embeda ADF Efficacy Form
- Hypothetical Example for Cost Impact Methods

Documents can be found at:
http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/drug-formulary-commission.html